

Appendiceal Carcinoma: Patterns of Failure Following Surgery and Implications for Adjuvant Therapy

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Background and Objectives: Primary adenocarcinoma of the appendix is rare, which makes an understanding of its natural history difficult. To date, it is treated predominantly with surgery alone. This review aims to elucidate the patterns of failure and treatment outcomes when adjuvant treatment is given after primary surgical resection.

Methods: Twenty-three patients were treated with either surgery alone, or with surgery and adjuvant radiation +/- chemotherapy. A review of the clinical course of these patients was undertaken with an analysis of the local control, distant failure, disease-free survival, and overall survival.

Results: Most patients presented with local invasion or metastatic disease often involving the peritoneum. Overall survival was 32%, similar to the results of other studies. Analysis of patients with locally advanced disease showed improvement in overall survival and local control with postoperative radiation therapy compared to surgery alone.

Conclusions: Adenocarcinoma of the appendix is a rare disease that presents most often in an advanced stage. It has been shown by others that a right hemicolectomy provides the best outcome with respect to surgical procedure. Postoperative irradiation appears to provide a benefit for both local control and overall survival.

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KEY WORDS: appendiceal cancer; radiation; hemicolectomy; chemotherapy

INTRODUCTION

Primary adenocarcinoma of the appendix is rare, representing < 0.5% of all gastrointestinal neoplasms [1], and it appears in 0.01–0.2% of appendectomy specimens [2,3]. The most common presentation is acute appendicitis [1,4–9]. A preoperative diagnosis has never been reported, and the diagnosis is rarely even suspected at the time of laparotomy [1,4,5,9,13].

Because the disease is rare, its natural history is poorly understood. Benefits from adjuvant radiation, chemotherapy, or a combination have not been reported. Most studies emphasize survival outcome based on surgical technique. To examine the patterns of failure and the effect of postoperative treatment in this disease, a review

was performed of patients who had undergone treatment for primary carcinoma of the appendix.

MATERIALS AND METHODS

For the period 1978–1997, 23 patients with primary appendiceal carcinoma were identified from the Massachusetts General Hospital Tumor Registry, and their medical records were reviewed. The mean age was 63 years, with a range of 34–88 years. Eleven patients were female, and 12 patients were male.

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Fourteen patients underwent right colectomy (61%), eight underwent simple appendectomy (35%), and one underwent exploratory laparotomy only (4%). Histologic examination was performed on the surgical specimens of all 23 patients and showed that eight (35%) tumors were adenocarcinomas and 15 tumors (65%) were mucinous adenocarcinomas.

Following surgery, five of the 15 patients with localized disease received postoperative irradiation to the tumor bed with concurrent 5-fluorouracil (5-FU) chemotherapy. A multifield technique was utilized with total doses of 43.2–50.4 Gy given with a mean of 45.5 Gy utilizing 1.8 Gy fractions [12]. Appropriate blocking and placement of clips during surgery to outline the tumor bed volume were utilized to minimize any potential toxicity to the small bowel and other normal tissues or organs such as the kidney or liver that may have been within the treatment fields. Only one patient received 5-FU-based chemotherapy alone following curative surgery.

Follow-up evaluations were at the discretion of the treating physician and could include physical examination, colonoscopy, and radiological evaluation with abdominal-pelvic CT scan, chest X-ray, and bone scan. All local failures were confirmed by laparotomy.

Statistical analysis using the Kaplan-Meier method was performed for local control, recurrence-free survival, overall survival, and distant failure for the entire study group of 23 patients and for the 15 patients within this group treated for cure.

RESULTS

For all 23 patients, the 5-year actuarial recurrence-free and overall survival was 32% and 35%, respectively (Fig. 1). Eight (35%) patients presented with metastases and 15 (65%) patients presented with locally advanced but nonmetastatic tumors. The clinical outcome of the 15 patients undergoing resection for locally advanced but nonmetastatic tumor was stratified by the use of postoperative irradiation.

All eight patients presenting with metastatic disease had diffuse peritoneal studding and died of disease within 1 year of presentation, and two of these patients also had involvement of the uterus and ovaries. Of the 15 patients with locally advanced disease, 14 (93%) patients had free intraperitoneal bowel perforation with microscopic residual disease present in seven (47%). Of the 12 patients with assessable lymph node status, three (25%) patients had nodal metastases.

Of the five patients undergoing resection and postoperative irradiation, three were alive without evidence of disease at 1 year, 4 years, and 5 years, respectively. One patient was alive at 1 year but developed local failure involving the ureter, and one patient died of carcinomatosis 4 years after treatment.

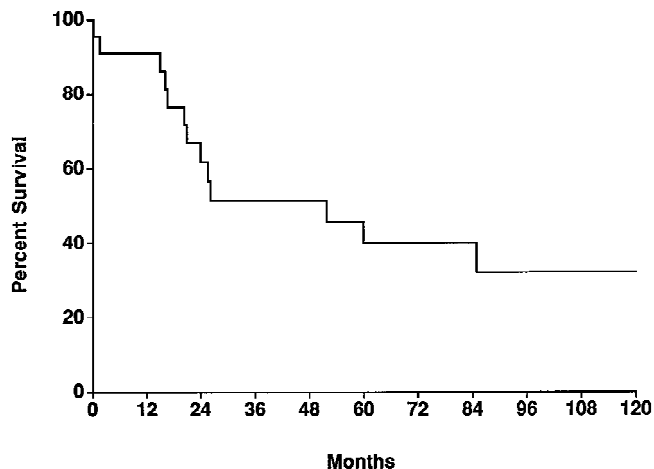


Fig. 1. Percent overall survival for all 23 patients with appendiceal carcinoma.

Of the nine patients undergoing resection without adjuvant therapy, one patient was alive and well at 6 years. One patient died postoperatively within 1 week from sepsis. The remaining seven patients died of their cancer within 2 years after surgery. Examination of patterns of recurrence showed that four developed local-regional failure only (two anastomotic recurrences, one regional nodal recurrence, and one retroperitoneal failure), and three patients developed metastatic disease only (two with peritoneal seeding and one with peritoneal seeding and liver metastases).

DISCUSSION

A high percentage of patients with adenocarcinoma of the appendix present with either locally advanced or metastatic disease [1,8,9]. In our series, spread to the peritoneum was the most common site, and patients who were able to be treated for potential cure had locally advanced disease. Most (14/15) had perforated appendices at laparotomy. Additionally, the majority of patients (12/15) who were treated for cure underwent a right hemicolectomy, which has been shown in several series to be the most effective procedure [1,4,7,10,11].

Patients with tumor-associated bowel perforation are at higher risk for local recurrence and may benefit from adjuvant irradiation and chemotherapy for both local control and survival [1,7,12,14]. Similarly, among our patients treated for cure, those receiving adjuvant treatment appeared to do better than those treated with surgery alone. Five of 10 patients failed locally after surgery alone, whereas only one of five failed locally after adjuvant irradiation. Three patients developed peritoneal metastases after treatment with surgery alone, but only one did so after surgery plus irradiation. Improved survival also appeared to result from adjuvant treatment, with only one of 10 patients who underwent surgery alone alive and well at last follow-up. However, four of the five

patients (80%) receiving postoperative treatment are alive, and three of these (60%) are without evidence of disease. Since metastases were predominantly within the abdomen and hematogenous spread was rare, radiation treatment to cover abdominal disease as part of curative treatment would seem appropriate.

Although patient numbers are small in this series, the results of the patients treated with surgery alone vs. surgery with adjuvant irradiation appear to show a benefit for those receiving postoperative treatment. Both local control and survival appeared to be enhanced with the addition of radiation, and therefore adjuvant treatment should be considered as a treatment option in this subset of colon cancer patients.

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